REMARKS

Claims 1-27, as amended, appear in this application for the Examiner's review and consideration. Claims 12-26 are currently withdrawn but will be rejoined when claim 1 is allowed. Claims 2 and 3 are cancelled and their contents have been incorporated into claim 1. The dependency of claims 4 and 5 has been changed. Claim20 has been amended to depend on a preceding claim (claim 16) instead of a later claim (claim 22) and to correct a typographical error. New claim 27 has been added to include part of the limitations in the original claim 9 which have been deleted in the currently amended claim 9. Claims 1 and 4-11 are presently pending for examination. The amended claims are supported by the specification and original claims so that their entry at this time is warranted. No new matter is being introduced.

In response to the Examiner's request for a new title, Applicants propose the following new title for the present invention: "Ig Heavy Chain Variants Expressed in Endothelial or Mesenchymal Cells and Uses Thereof". As disclosed in paragraphs [0100] and [0102] of the published application, Applicants have detected, in endothelial and mesenchymal cells, the expression of the Ig heavy chain variants, which were thought to be exclusive to B-lymphocytes until the Applicants' discovery. Furthermore, the application also teaches the diagnostic and therapeutic uses of the sequences of these Ig heavy chain variants in cell transfection, as antisense RNA and in the inhibition of tumor growth. Thus the new title is descriptive and highly indicative of the invention to which the claims are directed.

Claims 1-11 are rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the enablement requirement for the reasons stated on pages 3-7 of the Office Action. Applicants acknowledge with appreciation the Examiner's statement that the specification is enabled for an isolated polynucleotide consisting of a truncated μ heavy chain of SEQ ID NOs:1, 3, 4, 5, and 6, or encoding a peptide consisting of SEQ ID NO:2, an antisense DNA molecule to said polynucleotides; an expression vector comprising said polynucleotides and a host cell comprising said vector. In response to reasons of rejection, Applicants have amended the open-ended "comprising" to "consisting of" in claims 1 and 4-5. Thus it is now clear that the claims only intend to include polynucleotides within the said structural group and reasonable correlation exists between the scope of the claim and the scope of enablement set forth.

The main reason of rejection as stated by the Examiner is that the application does not provide "sufficient guidance in the specification as filed as to how the skilled artisan would make the various polynucleic acids recited in the instant claims". Applicants respectfully disagree. First, Applicants have provided a variety of examples of transcripts consisting of Ig heavy chain constant (Cμ) and joining region sequences and a 5' intronic J sequence upstream of the J region sequence including an in-frame methionine codon. Second, Applicants have demonstrated that the transcripts are expressed in the endothelial and mesenchymal cells. Third, as explained in paragraph [0100] of the published application, Applicants have taught various Cμ truncations, including transmembrane and secreted forms and the use of the sequences in cell transfection, as antisense RNA and in the inhibition of tumor growth. Most importantly, because the repertoire of Ig heavy chain constant (Cμ) and joining region (J) genes is of finite number, one of skill in the art would be able to practice the invention as claimed without undue experimentation. Based on the foregoing, Applicants believe that they have provided enablement for "any isolated polypeptide consisting of a transcript of an Ig gene, the polynucleotide lacking V region sequence and consisting of a constant domain and joining region sequences and a 5' intronic J sequence upstream of the J region sequence and including an in frame Met codon as claimed in claim 1".

Applicants also disagree with the Examiner's statement that "the instant fact pattern fails to indicate that representative number of structurally related compounds is disclosed" and "the artisan would not know the identity of a reasonable number of representative compounds falling within the scope of the instant claims and consequently would not know how to make them". As reasoned above, because the repertoire of Ig heavy chain constant (Cμ) and joining region (J) genes is of finite number, one of skill in the art would be able to identify the number of the representative compounds falling within the scope for the instant claims and know how to make them following the guidance provided in the application without undue experimentation.

The Examiner is correct in stating that finding a product is not equivalent to a positive recitation of how to make a product. However, the present application does not only disclose the discovery of members of the Ig family in mesenchymal and endothelial cells, it also provides detailed information (paragraph [0100] of the published application) regarding the isolation of the claimed polynucleotides so as to provide guidelines for the artisans to make and use the invention.

The Examiner is correct in pointing out that Applicants acknowledge that **unexpectedly** the MBA-13 mesenchymal stromal cell line, but not the negative control, was found to consistently

express TCRβ constant region. But the word "unexpectedly" in the context of the application is used to describe the unpredictable nature of the location of the expression of the Ig family members discovered by the inventors, not the structural and functional differences between the members of the Ig family proteins as interpreted by the Examiner. As the Examiner pointed out, not all sequence related proteins have similar properties. But in the vast majority of the cases, sequence similarities predict structural and functional similarities, which is the rationale behind categorizing proteins into families based on their sequence similarities. Although it is prudent to keep the possible exceptions in mind when working with newly identified protein families, it is unnecessary for the Ig family because proteins in the Ig family have been extensively studied and it is well known in the art that they have conserved tertiary structures. At least to this extent, the invention is considered to be predictable. Thus it is reasonable for Applicants to describe a genus of polynucleotide sequences consisting of a transcript of an Ig gene, lacking V region sequence and consisting of a constant domain and joining region sequences, a 5' intronic J sequence upstream of the J region sequence and an in-frame Met codon and therapeutic uses thereof, by reciting a representative number of polypeptide sequences (SEQ ID NOs 1, 3, 4, 5 and 6) defined by amino acid sequence, falling within the scope of the genus, and of structural features common to the genus, which features constitute a substantial portion of the genus.

To further demonstrate that the claimed invention is enabling, Applicants provide herein a declaration under 37 CFR 1.132. Using the isolation and characterization of stro-μ as an example, the inventors show that anyone skilled in the art should be able to make and use the proposed species of Ig genes by: (1) testing the expression pattern with RT-PCR; (2) confirming the expression pattern with Northern blot analysis; (3) verifying the translation of the transcript of the said Ig gene by Western blot analysis of the peptide encoded by the said Ig gene; (4) testing the function of the said Ig gene in treating cancer by transfecting human tumor cells with the said Ig gene and analyzing the induction of G1 phase arrest and differentiation of the transfected tumor cells. Thus, Applicants provide compelling evidence that the invention as presently claimed is enabling. In view of the foregoing, Applicants respectfully request that the non-enablement rejection be withdrawn.

In view of the above, the entire application is believed to be in condition for allowance, early notification of which would be appreciated. Should the Examiner not agree, a personal or telephonic interview is respectfully requested to discuss any remaining issues in order to expedite the eventual allowance of the claims.

Respectfully submitted,

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